

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1 (currently amended): A protein comprising an immunoglobulin heavy chain (HC) variable domain ~~sequence~~ and an immunoglobulin light chain (LC) variable domain ~~sequence~~, wherein the HC variable domain ~~sequence~~ and the LC variable domain ~~sequence~~ form an antigen binding site that binds to an activated conformation of LFA-1, wherein the protein has one or more of the following properties:

(i) the heavy chain variable domain ~~sequence~~ comprises:

- (a) a CDR1 that comprises ~~at least 3 amino acids from~~ RYVMW (SEQ ID NO: 1)
- (b) a CDR2 that comprises ~~at least 13 amino acids from~~ YIWPSGGNTYYADSVKG (SEQ ID NO:2); and/or
- (c) a CDR3 that comprises ~~at least 8 amino acids from~~ SYDFWSNAFDI (SEQ ID NO:3);

(ii) the light chain variable domain ~~sequence~~ comprises

- (a) a CDR1 that comprises ~~at least 7 amino acids from~~ RASQSIGSYLN (SEQ ID NO:7);
- (b) a CDR2 that comprises ~~at least 4 amino acids from~~ AASSLQS (SEQ ID NO:8); and/or
- (c) a CDR3 that comprises ~~at least 5 amino acids from~~ QQSYSTPS (SEQ ID NO:9);

(iii) the heavy chain variable domain ~~sequence~~ comprises a sequence at least 85% identical to the heavy chain variable domain sequence of the D2-57 SEQ ID NO:23, ~~DX-2001~~ SEQ ID NO:25, C1-54 SEQ ID NO:27, or P1-G10 SEQ ID NO:29 antibody;

(iv) the light chain variable domain ~~sequence~~ comprises a sequence at least 85% identical to the light chain variable domain sequence of the D2-57 SEQ ID NO:22, ~~DX-2001~~ SEQ ID NO:24, C1-54 SEQ ID NO:26, or P1-G10 SEQ ID NO:28 antibody;

(v) the heavy chain variable domain ~~sequence~~ comprises a sequence encoded by a nucleic acid that hybridizes under high stringent conditions to a sequence that

encodes the heavy chain variable domain ~~sequence of the D2-57, DX-2001~~ SEQ ID NO:42, C1-54 SEQ ID NO:43, or P1-G10 SEQ ID NO:44 antibody;

(vi) the light chain variable domain ~~sequence~~ comprises a sequence encoded by a nucleic acid that hybridizes under high stringent conditions to a sequence that encodes the light chain variable domain ~~sequence of SEQ ID NO: 42 the D2-57, DX-2001, C1-54~~ SEQ ID NO:43, or P1-G10 SEQ ID NO:44 antibody; and/or

(vii) the protein which competes with an antibody ~~D2-57, DX-2001, C1-54, or P1-G10~~ selected from the group consisting of

a) an immunoglobulin heavy chain variable domain sequence comprising SEQ ID NO:23, and an immunoglobulin light chain variable domain sequence comprising SEQ ID NO:22;

b) an immunoglobulin heavy chain variable domain sequence comprising SEQ ID NO:25, and an immunoglobulin light chain variable domain sequence comprising SEQ ID NO:24;

c) an immunoglobulin heavy chain variable domain sequence comprising SEQ ID NO:27, and an immunoglobulin light chain variable domain sequence comprising SEQ ID NO:26; and

d) an immunoglobulin heavy chain variable domain sequence comprising SEQ ID NO:29, and an immunoglobulin light chain variable domain sequence comprising SEQ ID NO:28;

for binding to activated LFA-1.

Claim 2 (currently amended): The protein of claim 1 that comprises at least the CDR regions of (i) and (ii) the D2-57-antibody.

Claim 3 (currently amended): The protein of claim 1 wherein the heavy and light chain variable domain sequences comprise, respectively, at least SEQ ID NO:23 and SEQ ID NO:22 ~~are at least 90% identical to corresponding variable domain sequences of the D2-57-antibody.~~

Claim 4 (currently amended): The protein of claim 1 ~~any of claims 1~~ wherein at least the

protein framework ~~80% of the FR regions are identical to FR sequence from a human germline sequence or a FR sequence of D2-57 SEQ ID NO:33 (heavy chain) and SEQ ID NO:36 (light chain); C1-54 SEQ ID NO:34 (heavy chain) and SE ID NO:37 (light chain);~~ or P1-G10.

Claim 5 (currently amended): The protein of claim 1 wherein the heavy chain variable domain ~~domains-sequence~~ comprises Xa-S-X2-D-X4-X5-S-X7-A-X8-X9-X10-X11 (SEQ ID NO:4), and

- (i) Xa is S or N;
- (ii) X2 is Y or F;
- (iii) X4 is hydrophobic;
- (iv) X5 is W or R;
- (v) X7 is N or Y;
- (vi) X9 is Y or F;
- (vii) X10 is D, E or A; and
- (viii) X11 is any amino acid.

Claim 6 (original): The protein of claim 1 that is not immunogenic in humans.

Claim 7 (original): The protein of claim 1 that is a full length IgG antibody.

Claim 8 (original): The protein of claim 1 that is an antigen binding fragment of an antibody, and does not include an Fc domain.

Claim 9 (original): The protein claim 1 that has at least a 20-fold preference for binding to activated LFA-1 relative to inactivated LFA-1.

Claim 10 (original): A protein comprising an immunoglobulin heavy chain (HC) variable domain sequence and an immunoglobulin light chain (LC) variable domain sequence, wherein

- (i) the HC variable domain sequence and the LC variable domain sequence form

an antigen binding site that binds to an activated conformation of LFA-1 ("aLFA-1");

(ii) the protein inhibits ICAM-1 binding to LFA-1 on human peripheral blood mononuclear cells with an IC_{50} of less than 5 nM.

Claim 11 (currently amended): A pharmaceutical composition that ~~comprising~~ comprises the protein according to any of claims ~~claim~~ 1-10 and a pharmaceutically acceptable salt.

Claim 12 (withdrawn): A method of treating or preventing inflammation or an inflammatory disorder, the method comprising: administering the protein of claim 1 to a subject in an amount effective to treat or prevent the inflammation or the inflammatory disorder.

Claim 13 (withdrawn): The method of claim 12 wherein the protein is administered at dosages less than 1 mg/kg per week, for at least 2 weeks.

Claim 14 (withdrawn): The method of claim 12 wherein the subject has psoriasis or is predisposed to psoriasis.

Claim 15 (withdrawn): The method of claim 14 wherein the subject has stable, plaque psoriasis.

Claim 16 (withdrawn): The method of claim 12 wherein the subject has or is predisposed to a disorder that is caused at least in part by a T cell inflammatory response.

Claim 17 (withdrawn): The method of claim 12 wherein the subject has or is predisposed to rheumatoid arthritis.

Claim 18 (withdrawn): A method of suppressing an immune response, the method comprising: administering the protein of 1 to a subject in an amount effective to suppress an immune response of the subject.

Claim 19 (withdrawn): The method of claim 18 wherein the subject has or is about to receive a transplant.

Claim 20 (withdrawn): The method of claim 18 further comprising administering a second agent that modulates T-cell function.

Claim 21 (withdrawn): The method of claim 20 wherein the second agent that modulates T-cell function is an antibody to CD154 or an antibody to CD45RB.

Claim 22 (withdrawn): A method of treating or preventing a disorder in a subject, the method comprising:

identifying a subject in need of an anti-LFA-1 antibody that preferentially binds to the activated form of LFA-1, but which subject does not respond or tolerate an anti-LFA-1 antibody that binds to activated and non-activated LFA-1 protein with substantially the same affinity; and

administering the anti-LFA-1 antibody that preferentially binds to the activated form of LFA-1, to the subject.

Claim 23 (withdrawn): A method of modulating aLFA-1 activity, the method comprising:

providing an aLFA-1-binding protein of claim 1; and

contacting the protein to aLFA-1, in an amount sufficient to modulate aLFA-1 activity.

Claim 24 (withdrawn): The method of claim 23 wherein the contacting is *in vitro*.

Claim 25 (withdrawn): The method of claim 23 wherein the contacting is *in vivo*.

Claim 26 (withdrawn): The method of claim 23 wherein the protein is contacted to aLFA-1 in the vicinity of a neoplastic cell.

Claim 27 (withdrawn): The method of claim 23 wherein the protein is contacted to aLFA-1 in the vicinity of an endothelial cell.

Claim 28 (withdrawn): A method for detecting the presence of an aLFA-1 protein, in a sample, in vitro, the method comprising:

(i) contacting the sample with an aLFA-1-binding protein according to any of claims 1-10, under conditions that allow interaction of the aLFA-1-binding protein and the aLFA-1 protein to occur; and

(ii) detecting interaction between the aLFA-1-binding protein, and the sample.

Claim 29 (withdrawn): The method of claim 28 wherein at least one of the aLFA-1 binding protein or the aLFA-1 is immobilized.

Claim 30 (withdrawn): A method for detecting the presence of activated LFA-1 in vivo, the method comprising:

(i) administering to a subject an aLFA-1-binding protein, under conditions that allow interaction of the aLFA-1-binding protein and the aLFA-1 protein to occur; and

(ii) detecting location of the aLFA-1-binding protein in the subject or formation of a complex between the aLFA-1-binding protein and aLFA-1 in the subject.

Claim 31 (withdrawn): The method of claim 30 wherein the subject is a human subject.

Claim 32 (withdrawn): The method of claim 30 wherein the detecting comprises imaging the subject.

Claim 33 (withdrawn): The method of claim 30 wherein the aLFA-1-binding protein is labeled with an MRI detectable label.